

**I. REMARKS**

Upon entry of the foregoing amendment, claims 1-14 and 17-20 are pending in the present application. Claims 15-16 were previously cancelled. Claims 9 and 18-20 stand withdrawn.

Applicants have amended claims 1-14 and 17-20 solely to advance prosecution. Applicants, by amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

It is believed this amendment does not introduce new matter and entry is respectfully requested.

**II. FINALITY OF LACK OF UNITY**

At pages 2-3 of the Official Action, the Examiner has indicated that the lack of unity has been maintained and has been made FINAL.

**RESPONSE**

In view of the finality of the lack of unity finding, applicants have amended the claims of this application so they are commensurate in scope with elected Group I. However, applicants respectfully take issue with the withdrawal of claim 9. Claim 9

clearly falls within elected Group I because R7 is a substituted phenyl. Group I is defined in the Official Action mailed February 2, 2009 as:

“Claims 1-14 and 17, drawn to compounds and pharmaceutical compositions of formula I wherein R2 and R3 do not combine to form a ring, none of the other R substituents form a ring, and R7 is a phenyl or a naphthyl.”

Applicants understand “a phenyl” and “a naphthyl” to encompass both unsubstituted and substituted varieties of these moieties. Indeed, a search of an unsubstituted phenyl would be coextensive with that of a substituted phenyl.

Again, applicants have deleted any recitation of the non-elected Het2 and R75-substituted Het2 in claim 9 to render the R7 substituent of claim 9 commensurate in scope with elected Group I.

Accordingly, applicants respectfully request rejoinder of withdrawn claim 9 and respectfully request favorable examination of claim 9 along with presently pending claims 1-14 and 17.

### **III. REJECTION OF CLAIMS 1-8, 10, 11 AND 17 UNDER 35 USC § 112, 1<sup>ST</sup> PARAGRAPH**

At page 2 of the Official Action, the Examiner has rejected claims 1-8, 10, 11 and 17 under 35 USC § 112, 1<sup>st</sup> paragraph as being non-enabled.

### **RESPONSE**

The rejection is respectfully traversed. However, solely to advance the prosecution of this application, applicants have presented amendments herein to the rejected claims.

In this regard, applicants note the Examiner's statement on page 3 that "the specification, while being enabling for substituents to be H, alkyl, alkoxy carbonyl alkyl, cyano, does not reasonably provide enablement for all the various substituents nor for the hydrates and hydrates of the salts thereof."

Regarding the "hydrates and hydrates of the salts thereof" language, applicants have amended the rejected claims to remove this language solely to advance prosecution.

Regarding the Examiner's statement about the enablement of the various substituents presently claimed, it is not entirely clear what the Examiner's statement means. Is the Examiner suggesting that all substituents are enabled for H, alkyl, alkoxy carbonyl alkyl and cyano even for those substituents that do not presently claim them? Is the Examiner suggesting that, only where these substituents are claimed, they are enabled? Is the Examiner suggesting that only these four substituents are enabled, even where the application clearly indicates that compounds have been actually synthesized that have substituents other than these four?

In any event, applicants respectfully submit that there are many more substituents presently claimed that are clearly enabled by the present specification in addition to those alleged are enabled by the Examiner. At a minimum, such compounds have been synthesized and/or there is clear direction on how to synthesize them, and should accordingly be viewed as enabled. See, for example, Table X on pages 61-62, Tables A1-A4 on pages 71-72 and Tables B1-B4 on pages 73-74, and Examples 1-69 on pages 79-86 of the present specification.

Applicants remind the Examiner that working examples, while not required to demonstrate enablement, are clear indicators of enablement, where present. The Examiner, however, on page 6 of the Official Action has erroneously stated that "the instant specification does not have any working examples". In contrast to the Examiner's erroneous statement, there are no fewer than 139 example compounds that have been synthesized.

Moreover, the Examiner has also stated at page 6 that "the inventor provides very little direction in the instant application". Applicants disagree with the Examiner's position regarding the amount of direction provided. The instant specification contains sufficient direction that would enable the ordinary skilled artisan to synthesize the presently claimed compounds. See the reaction schemes and other disclosure at pages 75-78 of the present specification.

Further, the Examiner has indicated on page 4 in her Wands factors analysis that "there is very little know (sic) in the regulation of fertility". Applicants

respectfully submit that all method claims 18-20 have been withdrawn as being directed to non-elected subject matter. It is not necessarily appropriate for the Examiner to now rely on allegations as to what is known in the "state of the prior art" regarding non-elected subject matter. Applicants respectfully submit that the Examiner should instead focus on the elected subject matter, i.e. the compound and composition claims.

Regarding the Examiner's statements on page 4 that "synthesizing compounds is very unpredictable" (see section 3) and "the pharmaceutical art is unpredictable" (see section 5), applicants submit that the Examiner has also conceded that the ordinary artisan in the pharmaceutical arts is "highly skilled" (see section 4). Based on the disclosure contained in the application as a whole, applicants respectfully submit that the amount of experimentation that may be required by the highly skilled person in the pharmaceutical arts to synthesize the presently claimed compounds is not undue.

Accordingly, applicants submit that the presently pending claims are clearly enabled by the instant specification. As such, reconsideration and withdrawal of this rejection is respectfully requested.

#### **IV. REJECTION OF CLAIMS 1-8, 10-14 AND 17 UNDER 35 USC § 103(a)**

Beginning at page 7 of the Official Action, the Examiner has rejected claims 1-8, 10-14 and 17 under 35 USC § 103(a) as being unpatentable over Zhang et al. (WO 2003/51877) in view of Bauser et al. (WO 03014117) and Bauser et al. (WO

03014116).

### **RESPONSE**

The rejection is respectfully traversed. The Examiner has not established a prima facie case of obviousness against the presently pending claims.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, there must be some motivation or teaching in the references cited by the Examiner to combine the separate elements taught in the separate references. As the U.S. Supreme Court held in *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." See *KSR International Co. v. Teleflex Inc. et al.*, 550 U.S. 398 at 417-418. Second, the

proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

The Examiner has stated that the difference between the presently claimed compounds and the cited references "is only in the substituents on the R5 phenyl ring". By this statement, it appears that the Examiner means that the presently claimed R5 substituent is different than the corresponding substituent on the Zhang et al. compounds, as well as each of the Bauser et al. compounds. In short, the Zhang et al. and Bauser et al. compounds all have a hydrogen at the 5-position of the tricyclic scaffold. In contrast, the presently amended claims may only have "1-4C-alkyl, cyano or 1-4C-alkoxycarbonyl" at the 5-position of the tricyclic scaffold. Applicants have canceled the possibility of R5=H from the presently pending claims.

However, the Examiner has indicated on page 12 of the Official Action that "compounds which have a close similarity in structure would be expected to have similar properties and hence motivating one to modify them to obtain new compounds. H vs. Me is not considered a patentable distinction absence evidence of superior unexpected results."

As such, applicants have submitted herewith a Declaration under 37 CFR §1.132 which demonstrates such "superior unexpected results" as requested by the

Examiner. In the Declaration, similar compounds were tested wherein R5 = H was substituted for a compound that falls within the scope of currently pending claim 1.

The Declaration clearly demonstrates that the compounds as claimed in presently pending claim 1 show a totally unexpected biological profile which by no means was suggested or implied by the compounds known from the art. In particular they show a superior pharmacological profile as PDE10 inhibiting compounds, since they unexpectedly show an increased potency regarding PDE10 inhibition and/or an increased selectivity for PDE10 over PDE4 when compared to compounds from the art where R5 is hydrogen.

These findings are completely unexpected in view of the teachings of the prior art which merely show that compounds of formula 1 with R5 being hydrogen are capable of inhibiting PDE10. As such, a person of ordinary skill in the art would not expect that replacing hydrogen in the R5 position by alkyl, alkoxycarbonyl, or cyano would lead to compounds with increased potency regarding PDE10 inhibition and/or an increased selectivity for PDE10 over PDE4.

As such, the presently rejected claims are unobvious over the cited references and withdrawal of this rejection is respectfully requested.



**V. PROVISIONAL REJECTION OF CLAIMS 1 AND 17 UNDER 35 U.S.C. §101 FOR  
STATUTORY DOUBLE PATENTING**

Beginning at page 13 of the Official Action, the Examiner has provisionally rejected claims 1 and 17 under 35 USC §101 as being unpatentable over USSN 10/562,149.

**RESPONSE**

The provisional rejection is respectfully traversed. The currently amended claims do not allow R5=H. In contrast, the '149 application only allows for R5=H.

Accordingly, the presently pending claims are not directed to the "same invention" as those presently pending in USSN 10/562,149.

Reconsideration and withdrawal of this provisional rejection is respectfully requested.

**VI. PROVISIONAL REJECTIONS OF CLAIMS 1-8, 10-14 AND 17 UNDER DOCTRINE OF  
OBVIOUSNESS-TYPE DOUBLE PATENTING**

At pages 14-15 of the Official Action, the Examiner has provisionally rejected claims 1-8, 10-14 and 17 under the doctrine of obviousness-type double patenting over USSN 11/794,497 and USSN 11/794,494.

**RESPONSE**

These provisional rejections are respectfully traversed. However, because all current rejections have been overcome with the amendments and remarks made herein, the Examiner must withdraw these provisional rejections because the '497 and '494 applications were filed much later than the presently pending application.

Reconsideration and withdrawal of these provisional rejections is respectfully requested.

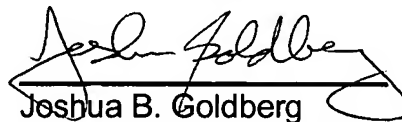
**VII. CONCLUSION**

Applicants assert that the claims are in condition for immediate allowance and early notice to that effect is earnestly solicited. Should the Examiner deem that any further action by Applicants' undersigned representative is desirable and/or necessary, the Examiner is invited to telephone the undersigned at the number set forth below.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

**THE NATH LAW GROUP**



Joshua B. Goldberg  
Registration No. 44,126  
Sheldon M. McGee  
Registration No. 50,454  
Customer No. 34375

Date: October 27, 2009  
**THE NATH LAW GROUP**  
112 South West Street  
Alexandria, Virginia 22314  
Tel: (703) 548-6284  
Fax: (703) 683-8396  
JBG/SMM/ROA.v2.doc